CLIPPER® HERBICIDE PRODUCT EVALUATION AND RECOMMENDATION

(June 2013)

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This document is a review of the aquatic herbicide Clipper® (EPA. Reg. No. 59639-161; Valent Biosciences Corp.). It contains product-specific aspects related to use characterization, inert formulation ingredients and adjuvants, and toxicity and effects of these ingredients to human health and non-target organisms. This document complements the MDAR/MassDEP review of the active ingredient flumioxazin (MDAR/MassDEP 2013).

1. Product Formulation

The product label indicates that the Clipper Herbicide is formulated as water dispersible granules containing 51% flumioxazin by mass (Valent Corp., 2012). The MSDS document indicates that the formulation also contains kaolin clay as a carrier at approximately 16% by mass. The identity of the other ingredients (also referred to as inerts) in Clipper Herbicide is considered proprietary; therefore, the manufacturer does not identify the other ingredients on the general or supplemental product labels or material safety data sheets (MSDS).

Proprietary information on the other formulation ingredients was obtained through a request for a Confidential Statement of Formula. The proprietary ingredients were evaluated as part of this review, but cannot be disclosed here for reasons of confidentiality.

The product label indicates that treatment of emergent vegetation requires the addition of spray adjuvants to the tank mix. As directed on the label, only adjuvants labeled for aquatic use should be utilized. Specific recommendations for adjuvants include those that contain non-ionic surfactants.

2 Use Characterization

2.1. Use Sites

The product label for the flumioxazin-formulated Clipper Herbicide specifies that this product may be applied for the control of vegetation in aquatic sites. Clipper Herbicide provides control of various submerged, emergent, and floating aquatic plants. The product may be applied directly to the water where there is limited or no outflow, including wetlands, lakes, fresh water ponds and reservoirs (Valent Corp., 2012).

2.2. Application Methods

Clipper Herbicide is applied as a water-based solution having a pH of 5 to 7. If treating floating or emerged weeds the addition of an adjuvant to the tank mix is needed. The product may be broadcast applied to the water surface or injected below the water surface. The label suggests that early morning applications may enhance weed control. The product may be applied by backpack or handgun sprayer, airboat, helicopter, airplane or other application equipment that is capable of thorough coverage of target plant foliage. Subsurface application may be done using weighted trailing hoses to ensure the release of the herbicide under the surface and throughout the biomass of aquatic vegetation. In situations where aquatic vegetation is dense, the label suggests that up to half of the water body be treated at a time to avoid a rapid decrease in dissolved oxygen caused by vegetation breakdown. It also notes that the remaining area of the water body can be treated 10 to 14 days later.

2.3. Use Rates

The label use rates per application of Clipper Herbicide are:

- Surface treatment at a rate of 6 to 12 ounces of formulated product per acre (0.375 to 0.75 lbs a.i./acre). The product should be applied in sufficient water volume to achieve adequate coverage of target vegetation.

- Subsurface application rates that produce 100 to 400 ppb of active ingredient in the water column. The product label provides information on the amount of product required per surface acre and water depth to achieve a desired water concentration. Application rates in waters greater than 7 ft deep should not exceed 14.8 lbs of product per surface acre. The label specifies a minimum retreatment interval is 28 days for a given section of a water body. In water bodies with a higher pH, efficacy of the herbicide is maximized by applications done early in the morning because lower pH values tend to occur at that time of the day.

2.4. Target Species

Clipper Herbicide is capable of controlling various submerged, floating, and emerged weed species. Floating and emerged weeds listed on the label include alligator weed, frog’s bit, water fern, water lettuce, water pennywort, and filamentous algae species. Submerged/floating weeds listed on the label include coontail, duckweed, fanwort, hydrilla, naiad, pondweed (curley, Illinois, sago, variable-leaf), water fern, water meal, and water milfoil (Eurasian, variable-leaf). A complete list of weeds controlled can be found on the product label (Valent Corp., 2012).

2. Human Health Effects of Other Ingredients

Both active and inert ingredients undergo scientific evaluation before approval by the USEPA. The agency must have sufficient data to make a safety determination regarding human health and the environment. For those inert ingredients applied to food, a tolerance or tolerance exemption is required. All food-use inert ingredients are also permitted for nonfood uses such as for ornamental plants, rights-of-way, aquatic use, structural use, etc.

Based on the information available on the US EPA website for pesticide inert ingredients[1], the inert ingredients in Clipper Herbicide are approved for both nonfood and food uses.

The chemical-by-chemical approach in risk assessment does not address mixture toxicity and thereby adds uncertainty. EPA's approach with toxicity assessment of mixtures is based on grouping of chemicals that exhibit their effects through a common mechanism. However, this is only applied to the cumulative risk assessments of active ingredients.

Adjuvants are generally broadly defined as any substance separately added to a pesticide product (typically as part of a spray tank mixture) that will improve the performance of the pesticide product. Since pesticide adjuvant products don't make pesticidal claims, they are not required to be registered. Where a product label directs the user to add a particular adjuvant before use, EPA will treat that adjuvant as an "other ingredient" in making the registration decision, and will assure that any necessary tolerances or exemptions from the requirement of a tolerance are established. However, it should be noted that residues of pesticide adjuvants in or on food commodities are subject to the requirements of the Federal Food, Drug and Cosmetic Act, which means that a food additive regulation or exemption from the requirement of a tolerance is needed for any substance used as a pesticide adjuvant that is applied to food crops. Adjuvant products used by aquatic vegetation management professionals in MA are recommended for aquatic use (Appendix 1).

4. Ecological Effects of Other Formulation Ingredients

The "inert" or "other" ingredients in the product formulation were not considered in the ecological risk assessment conducted by EPA. As mentioned above, all inert ingredients in pesticide products undergo scientific evaluation before approval for use by the EPA. The Agency must have sufficient data to determine that the use of the product will not cause unreasonable adverse effects to the environment. The inert ingredients in Clipper Herbicide have all been approved for application on nonfood and food sites.

For the purpose of the review presented here, the risks of the other formulation ingredients to aquatic non-target organisms were evaluated based on the consideration of toxicity information and concentrations in the formulation. It was concluded that these compounds are of a nature and/or present at levels in the product such that use of it as directed would not cause adverse aquatic ecological effects.

The combined effect of multiple substances was assessed by using the concentration additions approach. The combined effect of multiple compounds or substances is calculated by summation of the concentration of each compound divided by an effect concentration for that compound. This approach is considered to provide a conservative estimate of the mixture effect with relatively small likelihood of underestimating effects due to interactions (Lydy et al., 2004; Junghaus et al., 2006; Belden et al., 2007; Backhaus and Faust, 2012). The concentration addition is commonly applied by the use of toxic units (TU). The TU is defined as the quotient c_i/ECx_i which rescales the absolute concentrations of substances to individual potencies. The combined effect is estimated by the summation of TUs. This approach was used in an assessment of the combined effect of flumioxazin and its degradates. The assessment was based

[1] Pesticide Inert Ingredients: http://www.epa.gov/opprd001/inerts/

on the AQUATOX-derived environmental concentrations and refined assessment of toxicity endpoints of the degradate 482-HA based on ECOSAR predictions (see also Appendix 4 in flumioxazin review). Only acute effects were evaluated here and therefore the APF and THPA degradates were not considered. The toxicity endpoints for the inert ingredients were obtained from the open literature and government review documents.

The results are shown in Appendix 2 and indicate that the combined effect to fish and algae is dominated by the effect of flumioxazin, with very small contributions from effects of the other ingredients. For invertebrates the contributions of other ingredient #4 (a surfactant) exceeds the contribution of flumioxazin. If one applies the level-of-concern (LOC) thresholds as used in ecological risk assessment by EPA, the LOC for acute high risk of 0.5 is not exceeded for fish and invertebrates, but the LOC for endangered species of 0.05 is exceeded. The LOC for effects to algae is exceeded due to high toxicity of flumioxazin.

The concentration addition approach is not recommended for assessment of chronic effects from exposure from mixtures (Backhaus and Faust, 2012). The differences in environmental fate, such as dissipation rates and partitioning behavior, also complicate the exposure assessment for longer exposure times. A chronic ecorisk evaluation was conducted of the active ingredient flumioxazin and its major degradates. Details of this risk assessment can be found in the flumioxazin review document (Section 3). The refined assessment indicated that the projected flumioxazin concentrations averaged over 21 days exceeded chronic LOC for fish, but not for invertebrates. The projected concentrations of the three major degradates did not exceed LOCs for aquatic organisms.

5. Risk Assessment of Adjuvants

The application of Clipper Herbicide to emergent and floating vegetation requires the addition of an adjuvant to the tank mix. The risk characterization of adjuvants that may be used with the application of this aquatic herbicide is can be found in **Appendix 1.** The assessment indicates that even at the high-end estimated spray volumes, the adjuvants commonly used with aquatic herbicides would not pose risk to aquatic organisms in general, but one could pose risk to endangered species. The Agri-Dex adjuvant that is used by aquatic applicators operating in Massachusetts did not exceed LOCs and poses the lowest risk among the four adjuvants that were evaluated.

6. Risk Mitigation

The product label includes a number of statements and instructions that mitigate risks to non-target organisms. In addition to these label instructions, MDAR and MassDEP have additional recommendations and restrictions, some of which supercede some to the label restrictions.

Label Language

The potential movement from the application area and risks to non-target organisms are addressed by product label statements, including the following:

Environmental Hazards

The herbicide may be hazardous to plants outside the treatment area. Do not apply to water except as specified on the label. Do not contaminate water when disposing of equipment wash waters or rinsate. Ensure that spray drift to non-target species does not occur.

Application Site Restrictions

Clipper herbicide is not to be applied to flowing water, intertidal or estuarine areas.

Treatment of Waters with Dense Vegetation

Treatment of water bodies with dense vegetation may result in rapid and extensive decomposition which in turn can result in loss of oxygen in water. A sudden decrease in oxygen can result in fish suffocation. Therefore, water bodies with dense vegetation should be treated in sections.

Application to Waters used for Irrigation

To prevent adverse effects on crops, water treated with Clipper Herbicide may not be used for irrigation purposes until at least five days *after application.*

Managing Off-Target Movement

To minimize spray drift, the label contains drift reduction advisory information to address various equipment- and weather-related factors that determine the potential for spray drift. The factors addressed on the label include control of droplet size, application height, swath adjustment, wind, temperature and humidity, and temperature inversions.

7. Recommendations and Massachusetts Use Restrictions:

The flumioxazin review prepared by MDAR and MassDEP has examined the environmental fate and non-target toxicological characteristics of flumioxazin when used as an aquatic herbicide. These characteristics have been synthesized in risk assessments for human health and pond ecology.

Flumioxazin has a number of positive environmental fate characteristics. It degrades relatively quickly, progressively through more polar, water soluble degradates. However, there seems to be a lack of knowledge of the fate of the major degradates (see section in the review on Uncertainties and Data Gaps). There is a general concern with aquatic herbicide uses for contamination of groundwater underlying treated ponds**.** However, water column fate data indicate that water concentrations of flumioxazin and its degradates over shorter and longer term durations would be below levels of human health concern for drinking water. Therefore concentrations potentially reaching groundwater would be even less given degradation processes that would work on the parent and degradates as they pass though sediments and travel with groundwater. Flumioxazin has relatively high, non-selective predicted aquatic toxicity to a range of aquatic organisms. Our evaluation focused on fish and invertebrates. Included are high risks of concern to endangered species in some cases and to other non-endangered species in other cases after both short and long-term exposures. Flumioxazin has a high, non-selective, acute toxicity to all plants (including endangered species) from terrestrial to planktonic unicellular to vascular aquatic plants.

For threatened and endangered species, flumioxazin has a high, non-selective, acute toxicity and poses a high risk to all plants from terrestrial to planktonic unicellular to vascular aquatic plants.

The toxicological database for flumioxazin has a number of data gaps and most importantly lacks toxicity studies conducted under natural light conditions which would permit the full expression of the photo-induced toxicity that the flumioxazin class of compounds is known for. For this reason, the risk estimates derived in the review with existing data are likely underestimates of the risks to aquatic organisms.

Given these considerations, we are recommending that the herbicide Clipper®, containing the active ingredient flumioxazin be allowed for control of nuisance aquatic vegetation in the Commonwealth with a number of restrictions which either are in addition to those on the product label or supersede those on the label:

- The maximum permissible application concentration should be 200 ug/L.
- In order to limit the spatial extent of non-target damage from the toxicity of flumioxazin, no more that ¼ of the water body may be treated in any one year. This will allow for subsequent repopulation of damaged areas from adjacent untreated waters.
- Applications taking place within ¼ of the water body should be staggered around and within the basin to ensure that natural recolonization of native plants may occur. Repeat treatments within a year should be limited to targeted treatments around shoreline structures (e.g., boat launches, docks, swimming beaches, dams, water intake pipes, etc.).
- Treated areas may not be retreated with flumioxazin or any herbicide with a similar mode of action (i.e., light dependent peroxidizing herbicide) in consecutive years in order to prevent the development of herbicide resistance in treated plants. The exception to this restriction is repeat targeted treatments in consecutive years around shoreline structures (e.g., boat launches, docks, swimming beaches, dams, water intake pipes, etc.).
- Flumioxazin should be excluded from use in State-listed aquatic species habitats, unless otherwise authorized in writing on a case-by-case basis by the MA Division of Fisheries and Wildlife pursuant to MA Endangered Species Act (321 CMR 10.14 or 10.18).
- Given concerns for the toxicity of flumioxazin to mussels and the absence of knowledge about the effects of flumioxazin on these organisms, we recommend that applicators survey for native freshwater mussels in lakes being treated during the first year of use of

flumioxazin-containing products and implement a monitoring program if mussels are present to determine if any impacts to survival or growth occur after treatment. The MA Division of Fisheries & Wildlife Natural Heritage & Endangered Species Program is available to consult with applicators about the design and implementation of such programs. Permits are necessary to collect and kill freshwater mussels in Massachusetts.

References

Backhaus, T. and M. Faust. 2012. Predictive environmental risk assessment of chemical mixtures: a conceptual framework. *Environ. Sci. Technol*. 46:2564-2573.

Belden, J.B., R.G. Gilliom, and M.J. Lydy, 2007. How well can we predict the toxicity of pesticide mixtures to aquatic life. *Int. Env. Assessment and Manag*. 3:364-372.

Junghans, M., T. Backhaus, M. Faust, M. Scholze, and L.H. Grimme. 2006. Application and validation of approaches for predictive hazard assessment of realistic pesticide mixtures. *Aquatic Toxicology* 76: 93-110.

Lydy, M., J. Belden, C. Wheelock, B. Hammock, and D. Denton. 2004. Challenges in regulating pesticide mixtures. *Ecology and Society* 9:1-15.

Massachusetts Departments of Agricultural Resources and Environmental Protection. 2013. Flumioxazin. Technical Review. Posted on Department of Agricultural Resources, Aquatic Vegetation Management website. http://www.mass.gov/eea/agencies/agr/pesticides/aquatic-vegetation-management.html

Valent USA Corporation, 2012. Clipper herbicide label and MSDS. Accessed at: http://www.valent.com/professional/products/clipper/label-msds.cfm

Appendix 1

Risk Assessment of Adjuvants Used with Aquatic Herbicides

The Clipper Herbicide label indicates that treatment of emergent or floating vegetation requires the addition of an adjuvant in the tank mix. The label suggests the use of nonionic surfactants at recommended manufacturer's rates.

The risk assessment of several adjuvant products that are commonly used with the application of aquatic herbicides is presented below.

Toxicity Characterization

The toxicity of adjuvants was considered in risk assessments of herbicide applications in estuaries in Washington State (Entrix, 2003) and San Francisco (Pless, 2005). Commonly used adjuvants included non-ionic alkylphenol ethoxylates and/or fatty acids (e.g., R-11®, X-77®), and crop-oil based concentrates (e.g., Agri-Dex®, Hasten®). On the basis of EPA toxicity criteria, the non-ionic alkylphenol ethoxylates (e.g., R-11®, X-77®) are moderately acutely toxic to aquatic species. The crop-oil based surfactants would be considered practically non-toxic. Smith et al. (2004) characterized the toxicity of four surfactants to juvenile rainbow trout and implications for their use over water. The 96-h LC_{50} values were 6.0 mg/L for R-11®, 17 mg/L for LI 700®, 74 mg/L for Hasten, and 271 mg/L for Agri-Dex®. The 96-h EC_{50}s (on-bottom gilling behavior) were 4.4 mg/L for R-11® and 17 mg/L for LI 700®.

Curran (2003) determined the toxicity of formulated herbicide product Arsenal Herbicide (a.i., imazapyr) with and without the adjuvants Agri-Dex® and Hasten® using juvenile rainbow trout. The 96-h LC_{50} value for Arsenal Herbicide without adjuvant was 77,716 mg/L. In systems containing Arsenal plus adjuvant, the 96-h LC_{50} was expressed as mg/L surfactant and were reported to be 113 mg/L for Hasten® and 479 mg/L for Agri-Dex®. These values were compared with the LC_{50} values for the surfactants alone which were 74 mg/L for Hasten® and 271 mg/L for Agri-Dex®. Since this source of information was a meeting abstract, no further evaluation of data was possible for the review presented here. The authors concluded that the data suggest that the Arsenal Herbicide formulation has low toxicity to juvenile rainbow trout, the toxicity the tank mixes is driven by the surfactants, and depending on the type of surfactant and its percentage in the tank mix, surfactants may pose greater hazard to non-target species than Arsenal Herbicide.

Adjuvants and surfactants were also considered in human health and ecological effects risk assessments of imazapyr use for controlling vegetation in riparian corridors (AMEC, 2009). The most frequently used adjuvants were identified to be Agri-Dex®, Dyne-Amic®, Class-Act® and R-11®. It should be noted that the assessment did not consider direct applications to water. Reference was made to a study by Smith et al. (2004), which was cited above. While toxicity data were reviewed, the document did not include a formal exposure and risk assessment for the adjuvants.

Additional adjuvants that have been reported to being used by applicators in Massachusetts include Cide-Kick and Cygnet Plus. These adjuvants contain *d*-limonene as the major surfactant. Limonene is slightly toxic to fish and aquatic invertebrates with LC_{50} values of 80 mg/L and 39 mg/L, respectively (USEPA, 1994).

Exposure Assessment

Pless (2005) considered several adjuvants as used in tank mixes in the ecological risk assessment. The environmental properties and toxicity of adjuvants were also considered with the assessment of imazapyr herbicide use in estuaries in Washington State (Entrix, 2003). Both reviews considered estimated adjuvant concentration in water in an estuary scenario. For the purpose of this special review presented here, the environmental concentration of two adjuvants Agri-Dex® and Hasten® was estimated in a pond scenario as described below.

It was assumed that the adjuvant was used in a 1% v/v concentration in the tank mix (the label requires >0.25%). It was further assumed that the application volume was 50 gallons per acre (label requirement is >5 gal for ground applications). A 1% v/v adjuvant concentration in the 50 gal spray volume would correspond to a 1.89 L adjuvant volume per acre. Based on the density of Agri-Dex (0.879 kg/L, Agri-Dex MSDS), this volume corresponds to 1.66 kg Agri-Dex adjuvant per acre. The peak concentration of Agri-Dex® in a 1-acre water body with a 1-foot depth can be calculated as follows: 1.66×10^6 mg / (4047 m^2 × 0.3048 m × 1000 L/m^3) = 1.35 mg/L. For the 6.56-feet (2-meter) and 3-feet depths the concentrations are 0.21 mg/L(mg/L) and 0.45 mg/L(mg/L), respectively. The values for the adjuvants Hasten®, Cide-Kick and Cygnet Plus are very similar for the same adjuvant concentration given that the density of these adjuvants are very similar compared to Agri-Dex (0.87-0.9 kg/L). It should be noted that these calculations assumed no interception by target vegetation and no sorption to sediment. The adjuvant concentrations calculated above are slightly lower than the values for adjuvant concentrations that were reported in Entrix (2003). Those calculations assumed a density of 1 kg/L, whereas the actual density of the adjuvant products Agri-Dex® and Hasten® is less than 1 kg/L.

The Clipper Herbicide label does not specify spray volumes for foliar treatments other than to apply in sufficient volume of water per acre to ensure adequate coverage. A reasonable high-end estimate for spray volume could be 50 gallons per acre. Consequently, a high-end estimated level of adjuvant would be 1.35 mg/L in a 1-ft deep pond as calculated above.

Risk Assessment

As pointed out in the review by Pless (2005), the toxicity of the herbicide/adjuvant mixture is driven by the surfactant. The risk quotients presented by Pless (2005), based on environmental concentrations in an estuary scenario, were in the range of 0.13-0.051. The higher value was determined in association with the adjuvant Hasten®. That value marginally exceeded the level of concern (LOC) of 0.05 for endangered fish. It was pointed out that the highest measured exposure was extremely conservative in that the pesticide was applied directly to the estuary sediment (mud flat) without interception by vegetation and measured 3 hours later in the first overflow.

For the consideration of the application in a pond, the estimated environmental concentrations (EECs) of the Agri-Dex® and Hasten® adjuvants were calculated above. These two adjuvants were selected based on the availability of toxicity data for product with adjuvant (Curran et al., 2003). The highest estimated concentration in a water body with 1-foot depth was 1.35 mg/L. Based on the 96-hr LC_{50} of 479 mg/L expressed as adjuvant (Curran et al., 2003) for the product plus adjuvant mixture, the risk quotient is 0.0028. For the Hasten® adjuvant, the risk quotient would be 0.012. For the limonene-based adjuvants Cide-Kick and Cygnet Plus, the risk quotient would be 0.016. These values are below levels of concern for aquatic species as established by USEPA (2011), the most sensitive for endangered species acute risk being 0.05.

Entrix (2003) conducted a risk assessment of four adjuvants that have uses with glyphosate- and imazapyr-based aquatic herbicides. In addition to Hasten® and Agri-Dex®, the LI 700® and R-11® were included in the exposure and risk assessment. Since the spray-volume requirements for glyphosate-based herbicide are higher compared to imazapyr-based herbicides, the risk quotients were evaluated as a function of spray volume. The risk quotients were based on the LC_{50} values for juvenile rainbow trout as reported by Smith et al. (2004). The same procedure was used here for the concentrations developed for a pond scenario as described in Section 5.2. Figure 1 shows that the R-11 adjuvant exceeds the most sensitive Level of Concern (LOC) over the entire application volume range considered, while the Hasten® and Agri-Dex® adjuvants do not exceed the most sensitive LOC even at the highest application volume. In the review by Entrix (2003), it is pointed out that glyphosate-based herbicides require large application volumes (up to 100 gal/acre for efficacy), while 5 to 20 gal/acre can be used for imazapyr-based herbicides to yield equivalent results. Consequently, imazapyr-based herbicide applications are associated with lower adjuvant exposures compared to glyphosate-based herbicides.

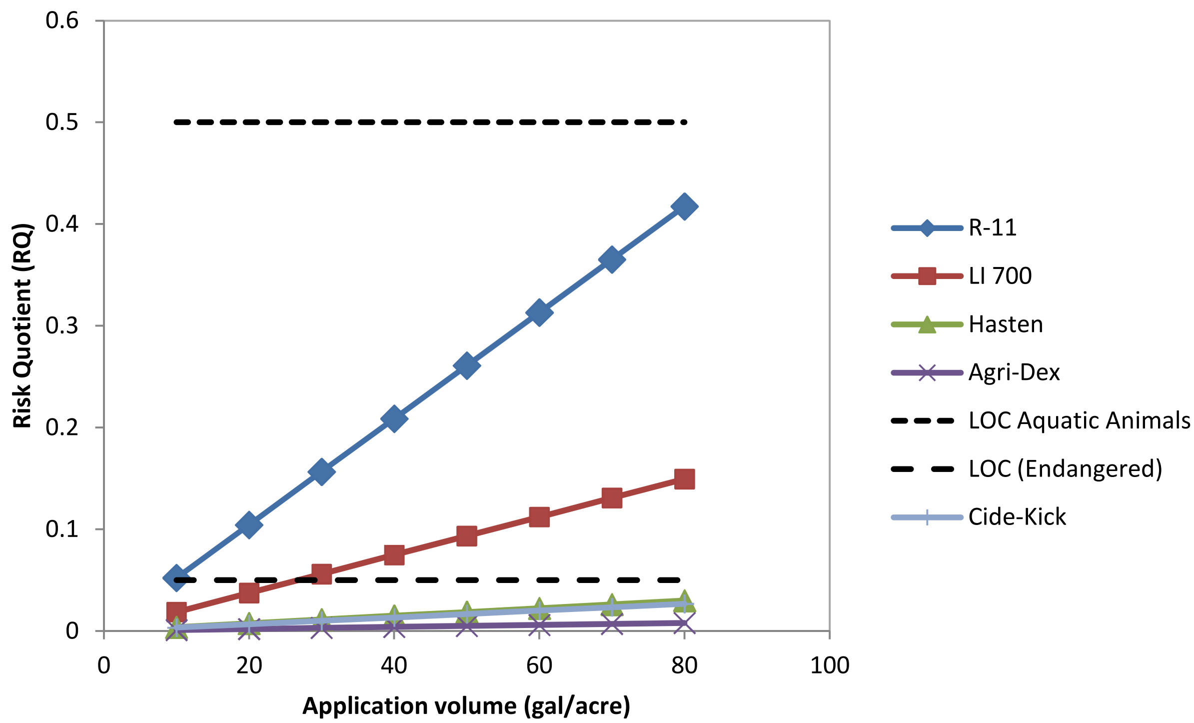

Figure 1. Risk quotient (RQ) of four spray adjuvants based on adjuvant concentrations associated with applications to a 1-foot deep water body. The adjuvant concentration was 1% v/v. The risk quotient was calculated based on the 96-h LC50 values for rainbow trout as reported by Smith et al. (2004) and USEPA (1994). The RQ values are compared with the Levels of Concern (LOC) for acute risk as developed by US EPA (2011).

Smith et al. (2004) estimated water depth at which the 96-h LC_{50} value for juvenile trout would be reached with an application volume of 20 gal/acre and labeled tank mix concentration (0.5 – 5%). The authors determined the water depths at which LC_{50} for the exposed trout would be reached. When used at the minimum recommended percentage of adjuvant in the tank mix the LC_{50} depth was <16 mm for R-11 and < 5 mm for the Agri-Dex®, Hasten® and LI 700®. At the maximum label recommended percentages of adjuvant in the tank mix, the LC_{50} depth for Agri-Dex would remain <5 mm, for Hasten it would be 10 mm and for LI 700 it would be 43 mm. It was concluded that Agri-Dex posed the lowest hazards to fish among the surfactants evaluated.

In the case of Clipper Herbicide, a high-end estimate of spray volume is 50 gal per acre. From the graph depicted in Fig. 1 above, it can be concluded that at that spray volume, even the R-11 adjuvant with the highest toxicity would not reach or even approach the LOC for aquatic animals, though it would exceed the LOC for endangered species. The LI700 adjuvant would not exceed the LOC for aquatic animals, but would exceed the LOC for endangered species. The Hasten, Agri-Dex and Cide-Kick adjuvants would not exceed the LOC for aquatic animals or endangered species.

References

AMEC, 2009. Human Health and Ecological Effects Risk Assessment, Imazapyr Risk Assessment Washington State. Prepared by AMEC Geomatrix, Inc., Lynwood, WA for Washington State Department of Agriculture, Olympia, WA. Available at: http://www.ecy.wa.gov/programs/wq/pesticides/seis/HHRA&ERA_063009.pdf

Curran, C. et al., 2003. Toxicity of Rodeo® and Arsenal® tank mixes to juvenile rainbow trout. University of Washington, Seattle, WA, USA. Meeting Abstract for SETAC 24th Annual Meeting.

Curran, C. A., J. M. Grassley, et al. (2004). "Toxicity of R-11® Surfactant to Juvenile Rainbow Trout: Does Size Matter?" Bulletin of Environmental Contamination and Toxicology **72**(2): 401-408.

Entrix, Inc. 2003. Ecological Risk Assessment of the Proposed Use of the Herbicide Imazapyr to Control Invasive Cordgrass (Spartina spp.) in Estuarine Habitat of Washington State. Prepared for Washington State Department of Agriculture, Project No. 3000901.

Pless, P. 2005. Use of Imazapyr Herbicide to Control Invasive Cordgrass (Spartina spp.) in the San Francisco Estuary: Water Quality, Biological Resources, and Human Health and Safety. Prepared for San Francisco Estuary Invasive Spartina Project. Prepared by Petra Pless, D.Env. Leson & Associates, Berkeley, CA.

Smith, B.C. et al., 2004. Toxicity of four surfactants to juvenile rainbow trout: Implications for use over water. Bull. Environ. Contam. Toxicol. 72:647-654.

USEPA, 1994. Reregistration Eligibility Decision: Limonene. Accessed at: http://www.epa.gov/oppsrrd1/REDs/3083.pdf

USEPA, 2011. Technical Overview of Ecological Risk Assessment. Accessed at: http://www.epa.gov/oppefed1/ecorisk_ders/toera_risk.htm

Appendix 2

Aquatic Toxicity Assessment of Clipper Herbicide Formulation

In order to assess the toxicity of combined exposure of active and other formulation ingredients, the toxic unit approach was used to estimate combined toxicity. The toxic unit approach is based on concentration addition. The combined effect of multiple compounds or substances is calculated by summation of the concentration divided by an effect concentration.

The concentration addition is commonly applied by the use of toxic units (TU). The TU is defined as the quotient c_i/ECx_i which rescales the absolute concentrations of substances to individual potencies. The combined effect is estimated by the summation of TUs.

The TU values were calculated for fish, aquatic invertebrates and algae. The results are shown in Fig. A2-1, A2-2, and A2-3 below. These results indicate that for fish and algae the combined effect is dominated by the effect of flumioxazin, with very small contributions from effects of the other ingredients. For invertebrates the contribution of other ingredient #4 (a surfactant) exceeds the contribution of flumioxazin.

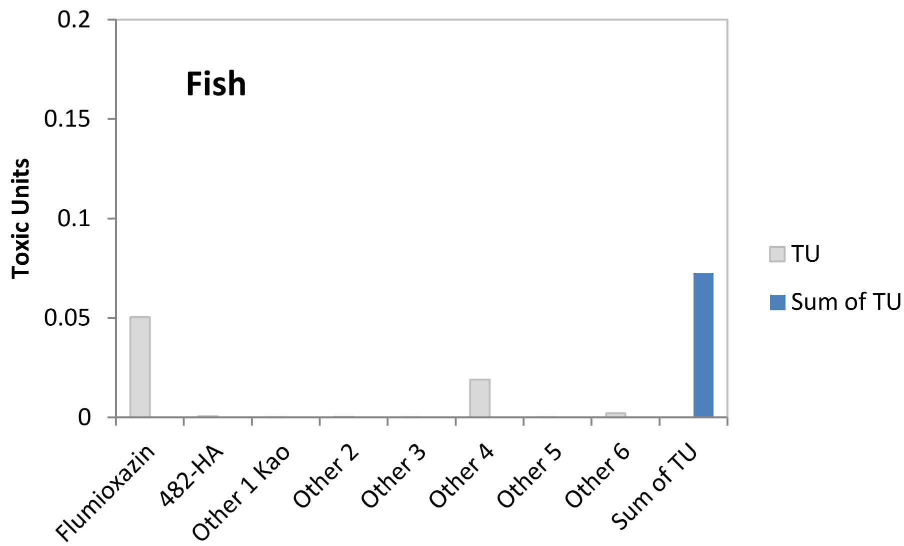

Figure A2-1 TUs of formulation ingredients for acute effects to fish

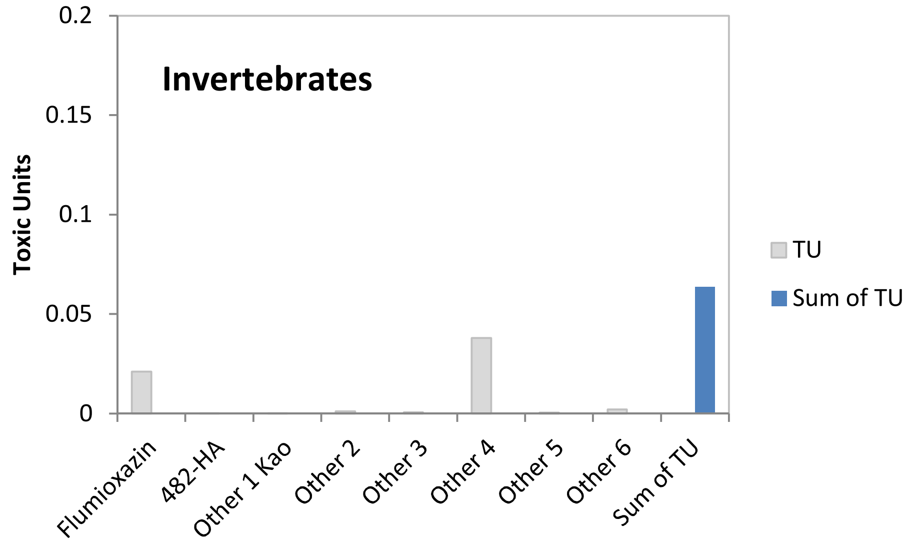

Figure A2-2 TUs of formulation ingredients for acute effects to aquatic invertebrates

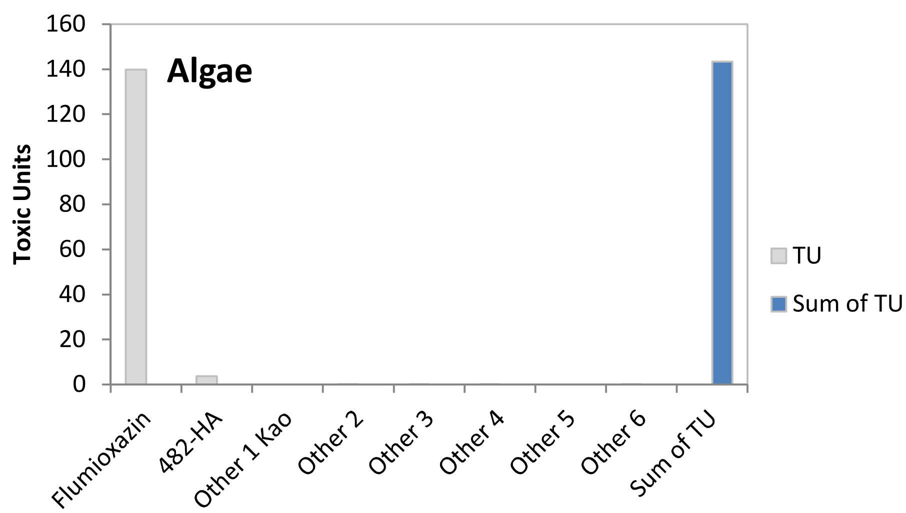

Figure A2-3 TUs of formulation ingredients for acute effects to algae

Spreadsheet with Toxic Unit (TU) calculations

Toxic Unit calculations for acute effects from exposure to Clipper Herbicide formulation ingredients. Information on the EECs and EC_{50}/LC_{50} for flumioxazin and the degradate 482-HA can be found in the review document for flumioxazin (MDAR/MassDEP, 2013, Section 3.1 and 3.2). The information on EECs and toxicity for the other ingredients is not disclosed here for proprietary reasons.

Ingredient	EEC mg/L	EC50/LC50 Fish mg/L	TU Fish	EC50 Aq. Invert. mg/L	TU Aq. Invert.	EC50 Algae mg/L	TU Algae
Flumioxazin	0.116	2.3	0.050435	5.5	0.021091	0.00083	139.759
482-HA	0.104	174	0.000598	493	0.000211	0.028635	3.631919
Other 1 Kao	0.121	1000	0.000121	1100	0.00011		
Other 2	0.038	100	0.00038	34	0.001118	54.3	0.0007
Other 3	0.004	50	0.00008	5.8	0.00069	14.7	0.000272
Other 4	0.019	1	0.019	0.5	0.038	0.5	0.038
Other 5	0.019	7300	2.6E-06	40	0.000475		
Other 6	0.015	7.3	0.002055	7.4	0.002027	4.8	0.003125
Sum of TU:			0.072671		0.063721		143.4331